Effect of cerebral protection strategy on outcome of patients with Stanford type A aortic dissection

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Objective: The aim of the present study was to assess the efficacy and mid- to long-term results of different cerebral protection techniques in the treatment of acute type A aortic dissection.

Methods: Between April 1987 and January 2011, 329 patients (220 male patients; median age, 60 years; range, 16-87) with type A aortic dissection underwent replacement of the ascending aorta or aortic arch with an open distal anastomosis. Either hypothermic circulatory arrest alone at 18°C (n = 116; 35%) or combined with retrograde cerebral perfusion (n = 122; 37%) or antegrade cerebral perfusion at 25°C (n = 91; 28%) was used.

Results: The median circulatory arrest time was 30 minutes (range, 12-92). The overall 30-day mortality was 19% (62 of 329). The 30-day mortality stratified by group was 26% (30 patients) in the hypothermic circulatory arrest group, 16% in the retrograde cerebral perfusion group (20 patients), and 13% (12 patients) in the antegrade cerebral perfusion group ($P = .047$). Permanent neurologic dysfunction occurred in 53 patients (16%), with statistically significant differences among the 3 groups (23% for hypothermic circulatory arrest, 12% for retrograde cerebral perfusion, and 12% for antegrade cerebral perfusion; $P = .033$). Univariate analysis showed a significant effect of the brain protection strategy on 30-day mortality and neurologic outcome. Multivariate analysis revealed preoperative hemodynamic instability, preoperative resuscitation, age, and operative year as independent predictors of 30-day mortality. Regarding permanent neurologic dysfunction, the multivariate analysis could not identify any independent predictors. Kaplan-Meier analyses revealed statistically significant differences among the 3 groups with a 1-, 3-, and 5-year survival rate of 84%, 79%, and 77% with antegrade cerebral perfusion, 75%, 72%, and 66% with retrograde cerebral perfusion, and 66%, 62%, and 60% with hypothermic circulatory arrest alone.

Conclusions: Patients in the antegrade cerebral perfusion group had the best short- and long-term survival rates. However, during the study period, several significant improvements in the treatment of patients with type A aortic dissection were achieved; therefore, independent predictors of mortality and permanent neurologic dysfunction were difficult to identify. (J Thorac Cardiovasc Surg 2013;146:647-55)

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Supplemental material is available online.

Acute aortic dissection type A is a devastating event associated with major morbidity and mortality requiring immediate surgical repair. The goal of surgical intervention is operative survival. To achieve this, the only causative option for patients with acute aortic dissection is replacement of the dissected ascending aorta to prevent myocardial ischemia and cardiac tamponade. The International Registry of Acute Aortic Dissection data reported an in-hospital mortality rate of 26% in the current era.[1] Cerebral protection during surgery is crucial for postoperative survival and positive neurologic outcomes.[2-4] During the past decades, various cerebral protection methods have been used. They have all been based on hypothermic circulatory arrest (HCA), which was introduced clinically by Griepp and colleagues[5] in 1975. In addition to HCA alone, cerebral perfusion strategies have been developed to prolong the safe duration of circulatory arrest. In 1986, selective antegrade perfusion of the brain with cold blood during surgery of the aortic arch was introduced by Bachet and colleagues.[6] Retrograde cerebral perfusion (RCP) was first used in dissection patients by Ueda and colleagues.[7] These techniques have been described in numerous published studies and have been widely used; however, data from large clinical trials are scarce.[8]

The present study was undertaken to compare the experience and results in patients undergoing surgery for acute type A dissection with 3 different cerebral protection methods at a single center. Particular emphasis was placed

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Abbreviations and Acronyms

ACP = antegrade cerebral perfusion
bACP = bilateral ACP
CPB = cardiopulmonary bypass
HCA = hypothermic circulatory arrest
PND = permanent neurologic deficit
RCP = retrograde cerebral perfusion
uACP = unilateral ACP

on mortality, both in-hospital and long-term, and neurologic outcome.

PATIENTS AND METHODS

The data from 329 patients with acute aortic dissection type A undergoing replacement of the ascending aorta or aortic arch with an open distal anastomosis at a single center (Department of Cardiac Surgery, Vienna Medical University) between April 1987 and January 2011 were prospectively collected and retrospectively analyzed. The demographic data are listed in Table 1.

Study Groups

The patients were categorized according to the cerebral protection method used into 1 of 3 groups: HCA alone (n = 116; 35%), HCA combined with RCP (n = 122; 37%), and HCA combined with antegrade cerebral perfusion (ACP; n = 91; 28%; Figure 1). The type of cerebral protection was at the surgeon's discretion for the whole study period.

Definitions

All cases of hemiplegia and paraplegia and every other neurologic deficit resulting from either central or peripheral neurologic damage that was still present at discharge from the hospital was defined as a permanent neurologic deficit (PND). Liver failure was defined as a significant increase in transaminases and an increase in prothrombin time of at least 10%. Near infrared spectroscopy was introduced as a neuromonitoring tool in 1998. Since then, it was used in 150 patients.

Operative Technique

All operations were performed by way of a median sternotomy. After patients had received heparin (330 IU/kg body weight), cardiopulmonary bypass (CPB) was established through either the femoral artery or right subclavian artery and the right atrium. In cases of tamponade, the strategy was chosen according to patient stability. In hemodynamically stable patients with beginning tamponade, CPB was established before sternotomy. In the case of hemodynamic instability and cardiac tamponade, sternotomy was performed before cannulation, and the heart was decompressed by a small incision into the pericardium.

Once CPB had been established, systemic cooling was immediately initiated. A left ventricular vent was placed through the right superior pulmonary vein, and a retrograde cardioplegia catheter was placed into the coronary sinus. For central neurologic protection, the patient's head was packed in ice bags, and 1000 mg of methylprednisolone was given before the onset of HCA. The ascending aorta was replaced with an open distal anastomosis, if the entry tear or acute type A dissection was located in the aortic root or aortic arch. Surgical therapy also included repair or replacement of the involved structures, such as the aortic valve, aortic root, and/or aortic arch. For HCA and RCP, CPB was stopped after the patient was cooled to the target esophageal temperature of 18°C. In the case of ACP, circulatory arrest was initiated at an esophageal temperature of 25°C.

Two different strategies were used to establish ACP. In the case of subclavian artery cannulation for CPB, we snared all supra-aortic arch vessels, including the brachiocephalic trunk, after securing adequate backflow. In the case of femoral artery cannulation for CPB, we inserted a cannula under direct vision into the brachiocephalic trunk, and snared the vessel afterward. In the case of bilateral ACP, the left carotid artery was selectively intubated and perfused after opening the arch. The brain was perfused with blood at a temperature of 25°C, with a flow rate of 10 mL/kg/min body weight. The lower body was kept in circulatory arrest. In the case of RCP, a 28F cannula was advanced into the superior vena cava, snared cranially of the azygos vein, and connected to the arterial line. Retrograde flow was slowly increased and regulated to achieve a target central venous pressure of 20 mm Hg. Maintenance of adequate retrograde flow volume required infusion of 500 to 1000 mL. This resulted in a median flow rate of 280 mL/min (range, 50-650).

Statistical Analysis

The data from the patients were analyzed using SPSS statistical software (PASW, version 18.0, for Macintosh; IBM Corp, Somers, NY). Categorical variables are presented as numbers and percentages and continuous variables as medians and ranges. For comparison of continuous variable, we used 1-way analysis of variance testing when 3 groups were compared and the Mann-Whitney *U* test when 2 groups were compared. Categorical variables were compared using the χ^2 test. Survival was compared using Kaplan-Meier analysis and log-rank testing. The most important factors influencing 30-day mortality and PND rates were entered in a binary regression model.

RESULTS

Demographic Data

The 3 groups did not differ significantly with respect to gender, preoperative neurologic deficit (including transient ischemic attack, prolonged reversible ischemic neurologic deficit, and stroke), coronary artery disease, myocardial infarction, previous cardiac surgery, cardiopulmonary resuscitation, and renal failure.

Rupture, hemodynamic instability, arterial hypertension, and pulmonary dysfunction were found more frequently in the HCA only and RCP groups. The RCP patients were significantly younger at surgery (Table 1).

Mortality and Neurologic Outcome

The overall 30-day mortality was 19% (62 of 329), with statistically significant differences among the different cerebral protection methods during circulatory arrest. The mortality was 26% in the HCA group (30/116), 16% in the HCA plus RCP group (20/122), and 13% (12/91) in the HCA plus ACP group ($P = .047$).

The predominant cause of death within 30 days was cardiac failure (n = 24) followed by multiorgan failure (n = 14), bleeding episodes (n = 9), neurologic complications (n = 7), sepsis (n = 5), and pulmonary failure (n = 2). In 1 patient, the cause of death was unknown (see Table E1).

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TABLE 1. Demographic data

Variable	Overall	HCA only	RCP	ACP	*P* value
Patients (n)	329	116	122	91	
Age at surgery (y)	60 (16-87)	60 (16-84)	56(18-87)	62 (33-85)	.043
Male gender	220 (67%)	82 (71%)	75 (62%)	63 (69%)	.273
Preoperative PRIND	2 (1%)	1 (1%)	0	1 (1%)	.530
Preoperative TIA	11 (3%)	4 (3%)	6 (5%)	1 (1%)	.320
Preoperative stroke	7 (2%)	3 (3%)	3 (3%)	1 (1%)	.730
Hemodynamic instability	60 (18%)	28 (24%)	25 (21%)	7 (8%)	.014
Rupture	147 (45%)	55 (47%)	69 (57%)	23 (25%)	<.001
Cardiopulmonary resuscitation	12 (4%)	5 (4%)	6 (5%)	1 (1%)	.674
Pulmonary dysfunction	70 (21%)	29 (25%)	33 (27%)	8 (9%)	.003
Myocardial infarction	18 (6%)	4 (3%)	9 (7%)	5 (6%)	.413
Coronary artery disease	49 (15%)	19 (16%)	20 (16%)	10 (11%)	.481
Arterial hypertension	279 (85%)	104 (90%)	107 (88%)	68 (74%)	.011
Renal failure	23 (7%)	6 (5%)	10 (8%)	7 (8%)	.618
Previous cardiac surgery	19 (6%)	7 (6%)	7 (6%)	5 (6%)	.986

Data presented as median (range) or number (%). *HCA,* Hypothermic circulatory arrest; *RCP,* retrograde cerebral perfusion; *ACP,* antegrade cerebral perfusion; *PRIND,* prolonged reversible ischemic neurologic deficit; *TIA,* transient ischemic attack.

Of the 329 patients, 53 (16%) developed PND: 27 (23%) in the HCA-only group, 15 (12%) in the RCP group, and 11 (12%) in the ACP ($P = .033$; Tables 2 and 3).

Long-term survival analyses also revealed significant differences among the 3 groups. The survival at 1, 3, 5, and 10 years was 66%, 62%, 60%, and 50% in the HCA-only group and 75%, 72%, 66%, and 51% in the RCP group, respectively; the 1-, 3-, and 5-year survival in the ACP group was 84%, 79%, and 77%, respectively (median follow-up, 63 months; range, 1-290; $P = .035$; Figure 2).

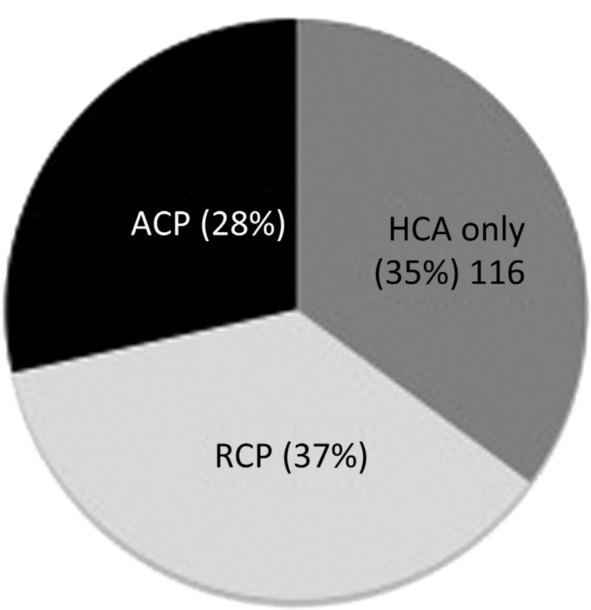

FIGURE 1. Percentage of use for 3 different cerebral protection strategies: hypothermic circulatory arrest (*HCA*) only (n = 116), retrograde cerebral perfusion (*RCP*) (n = 122), and antegrade cerebral perfusion (*ACP*) (n = 91).

Unilateral Versus Bilateral ACP

In 53 (58%) of the 91 ACP patients, cerebral perfusion was performed unilaterally (uACP) and in 38 (42%), bilaterally (bACP; Figure 3). A subgroup analysis between those 2 groups was performed. The 30-day mortality for the uACP patients was 19% (10 of 53) and was 5% (2 of 38) for the bACP patients ($P = .059$). The circulatory arrest time was slightly longer for the bACP group (29 minutes, range, 11-74; vs 33 minutes, range, 15-113; $P = .023$). The PND rates were comparable in both groups (uACP, 7 [14%]; and bACP, 4 [11%]; $P = .699$). The incidence of postoperative renal failure rate (requiring dialysis) was greater in the bACP group than in the uACP group (12 [32%] vs 5 [9%], respectively; $P = .0173$; Table 4).

Kaplan-Meier analysis revealed no significant differences in long-term survival between the bACP and uACP groups (1-, 3-, and 5-year survival rate, 90%, 81%, and 73% vs 79%, 77%, and 77%, respectively; $P = .885$). The median follow-up was 43 months (range, 1-108; Figure 4).

Risk Factors for Perioperative Mortality

A comparison of the data from the patients who survived 30 days postoperatively and those who died revealed that the nonsurvivors were significantly older (median age, 65 years; range, 32-84; vs 59 years; range, 16-87; $P = .023$), were more frequently hemodynamically unstable preoperatively (44% vs 12%, $P < .001$), required resuscitation more often (16% vs 1%, $P < .001$), and had a significantly greater rate of aortic rupture (58% vs 42%, $P = .019$). The CPB time, aortic crossclamp time, and length of circulatory arrest were slightly longer among the nonsurvivors. Finally, HCA only was used more frequently in nonsurvivors (32% vs 48%; $P = .016$), with

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TABLE 2. Intraoperative data

Variable	Overall	HCA only	RCP	ACP	*P* value
Patients (n)	329	116	122	91	
CPB time (min)	180 (101-404)	177 (101-355)	198 (121-404)	161 (101-303)	<.01
Crossclamp time (min)	109 (61-230)	107 (61-203)	114 (62-230)	109 (61-179)	<.037
Circulatory arrest time (min)	30 (12-92)	36 (12-88)	30 (14-88)	30 (14-92)	.993
Cooling time (min)	56 (18-162)	51 (26-132)	63 (30-162)	47 (18-150)	<.01
Aortic valve surgery	98 (30%)	44 (38%)	33 (27%)	21 (23%)	.052
David operation	6 (2%)	2 (2%)	2 (2%)	2 (2%)	.951
Complete arch	7 (2%)	0	3 (3%)	4 (4%)	.089
Composite graft	57 (17%)	25 (22%)	19 (16%)	12 (14%)	.317
"Elephant trunk"	2 (1%)	1 (1%)	1 (1%)	0	.680
Stent graft	22 (7%)	7 (6%)	6 (5%)	9 (10%)	.335
Mitral valve surgery	3 (1%)	1 (1%)	1 (1%)	1 (1%)	.975
CABG	27 (8%)	11 (10%)	10 (8%)	6 (6%)	.754
Reoperation	94 (29%)	29 (25%)	44 (36%)	21 (23%)	.083

Data presented as median (range) or number (%). *HCA,* Hypothermic circulatory arrest; *RCP,* retrograde cerebral perfusion; *ACP,* antegrade cerebral perfusion; *CPB,* cardiopulmonary bypass; *CABG,* coronary artery bypass grafting.

only 19% receiving ACP compared with 30% of survivors ($P = .069$; Table 5).

Multivariate analyses revealed preoperative hemodynamic instability, cardiopulmonary resuscitation, patient age at surgery, and operative year as independent predictors of 30-day mortality (Table 6). The operative year reached significance ($P = .048$) but only with a regression coefficient of –0.074 and an odds ratio of 0.929.

Risk Factors for PND

No significant demographic differences were found among patients with a PND. In patients with PND, HCA only had been used more frequently (51% vs 32%, $P = .008$). Also, more patients with a PND required surgical revision (45% vs 25%. $P = .006$; Table 7). In the multivariate regression model, adding the operative year as a continuous variable removed every significant influence of any factor; thus, not HCA nor previous cardiac surgery nor operative year was an independent factor in our analysis (Table 8).

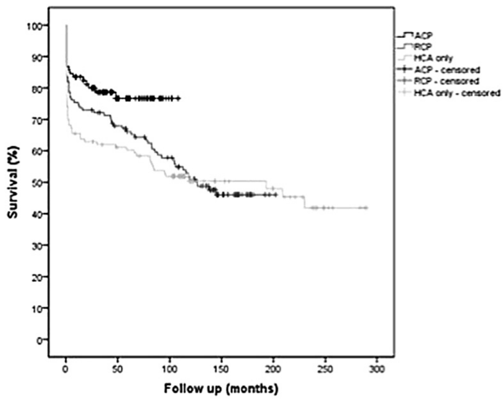
Developments in Type A Aortic Dissection Treatment

The study period was 24 years from April 1987 to January 2011, and, in addition to ACP and RCP, a number of other significant improvements were achieved, including earlier and better diagnosis, a quicker referral to surgery, and better anesthetic management. We stratified the patients according to the era of surgery for type A aortic dissection into 3 groups: 1987 to 1996 (period 1), 1997 to 2004 (period 2), and 2005 to 2011 (period 3). These periods were selected according to the introduction of new techniques, with a certain overlap. A comparison of the pre- and intraoperative patient characteristics showed that the rates of preoperative hemodynamic instability (22% vs 21% vs 9%, $P = .052$) and aortic rupture (43% vs 58% vs 22%, $P < .001$) decreased significantly

TABLE 3. Postoperative data

Variable	Overall	HCA only	RCP	ACP	*P* value
Patients (n)	329	116	122	91	
30-d Mortality	62 (19%)	30 (26%)	20 (16%)	12 (13%)	.047
Ventilation time (d)	3 (1-79)	3 (1-54)	4 (1-79)	2 (1-45)	.168
ICU stay (h)	6 (1-86)	5 (1-73)	7 (1-86)	5 (1-62)	.041
PND	53 (16%)	27 (23%)	15 (12%)	11 (12%)	.033
TIA	3 (1%)	1 (1%)	0	2 (2%)	.253
Liver failure	8 (2%)	5 (4%)	3 (3%)	0	.130
Renal failure (requiring dialysis)	53 (16%)	20 (17%)	16 (13%)	17 (19%)	.454
Multiorgan failure	25 (8%)	11 (10%)	13 (11%)	1 (1%)	.023
Reintubation	23 (7%)	9 (8%)	12 (10%)	2 (2%)	.866
Sepsis	39 (12%)	23 (20%)	12 (10%)	4 (4%)	.002
Hospital stay (d)	19 (3-96)	19 (5-77)	20 (5-96)	17 (3-88)	.522

Data presented as number (%) or median (range). *HCA,* Hypothermic circulatory arrest; *RCP,* retrograde cerebral perfusion; *ACP,* antegrade cerebral perfusion; *ICU,* intensive care unit; *PND,* permanent neurologic deficit; *TIA,* transient ischemic attack.



Survival rates:

	1-years	3-years	5-years	10-years
HCA only	66%	62%	60%	50%
RCP	75%	72%	66%	51%
ACP	84%	79%	77%	n.a.

Patients at risk

	1-years	3-years	5-years	10-years
HCA only	75	69	66	30
RCP	91	85	73	51
ACP	73	52	39	n.a.

FIGURE 2. Kaplan-Meier survival analysis curves for antegrade cerebral perfusion (*ACP*) versus retrograde cerebral perfusion (*RCP*) versus hypothermic circulatory arrest (*HCA*) only (log rank, $P = .035$; median follow-up, 63 months; range, 1-290).

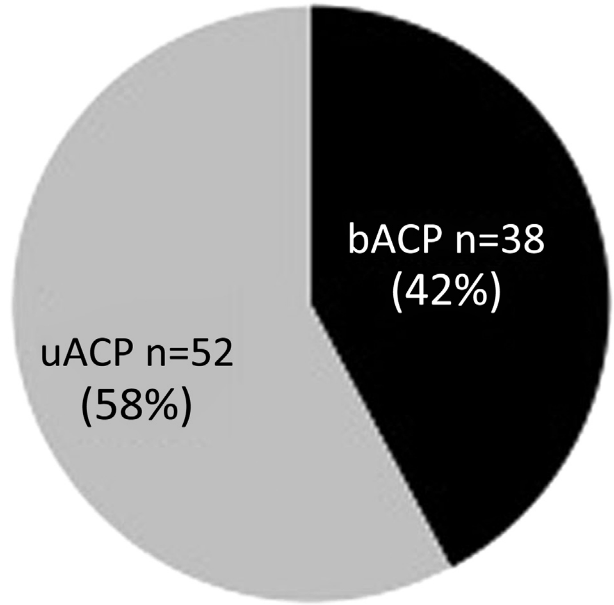


FIGURE 3. Percentage of patients in antegrade cerebral perfusion (*ACP*) group perfused either unilaterally (*uACP*) or bilaterally (*bACP*).

during the study period, especially for the last group (Table 9). Although this difference was statistically significant in the case of aortic rupture, it did not reach significance for hemodynamic instability. The rate of preoperative cardiopulmonary resuscitation remained the same for all 3 periods. A comparison of the cerebral protection strategies revealed HCA only as the main strategy for period 1 (74%), with 26% receiving RCP. During period 2, RCP was the dominant strategy (56%), with HCA only decreasing to 27% and ACP, which was not known in period 1, emerging as a new treatment modality (16%). In period 3, ACP had become the method of choice (76%), with HCA only (11%) and RCP (13%) used only occasionally ($P < .001$).

Both mortality and the incidence of PND decreased significantly during the study period. The 30-day mortality was 31% in period 1, 16% in period 2, and 11% in period 3 ($P = .001$). The corresponding PND rates were 27%, 13%, and 11% ($P = .007$). Kaplan-Meier analysis revealed a 1-, 3-, 5-, and 10-year survival rate of 56%, 51%, 49%, and 34% in period 1 compared with 77%, 73%, 70%, and 59% in period 2, respectively. By contrast, the 1-, 3-, and 5-year survival rate in period 3 was 87%, 85%, and 82%, respectively ($P < .001$; Figure 5).

DISCUSSION

Taken together, our data indicate that the outcome of surgical treatment of type A dissection at our center has improved over time and that ACP at hypothermic circulatory arrest yields the best results with regard to mortality and PND.

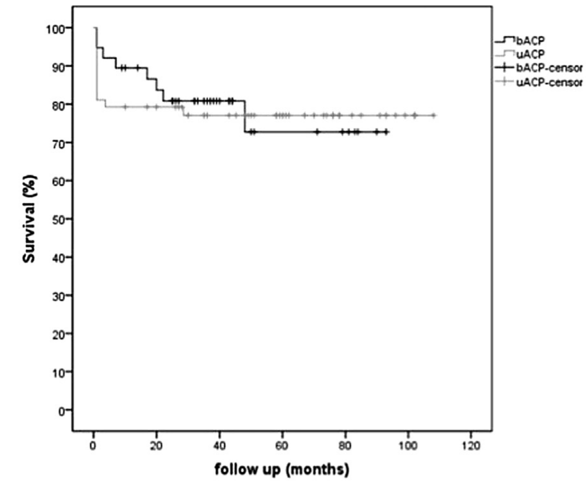
Acute dissection of the aorta was first described in detail in 1760 when King George II died of this condition.[9] It is a catastrophic event that represents a formidable surgical challenge. Without surgery, 50% of patients die within the first 48 hours, and the 2-week mortality rate approaches 80% in patients with undiagnosed or untreated ascending aortic dissection.[1,10,11] With improved preoperative diagnosis, better prosthetic material, amelioration of cardiac and cerebral protection, and increased surgical experience, the results have improved during the past 20 years.[12,13] However, the average mortality in most registries remains 20% to 25%.[2,14,15]

Surgical treatment of type A aortic dissection consists primarily of replacement of the ascending aorta to exclude the entry tear and prevent expansion of the dissection toward the aortic root and rupture into the pericardial sac. In about 10% of patients, the aortic root is involved, and 5% of the patients require replacement of the entire aortic arch. Deep HCA is the most commonly used method of cerebral protection during surgery of the aortic arch. However, this technique offers only a limited period for arch repair. Also, it requires prolonged CPB to rewarm the patient,

TABLE 4. Subgroup analysis of unilateral ACP vs bilateral ACP

Variable	uACP	bACP	*P* value
Patients (n)	53 (58%)	38 (42%)	
CPB time (min)	165 (101-303)	157 (102-285)	.243
Aortic crossclamp time (min)	109 (62-166)	95 (61-179)	.717
Circulatory arrest time (min)	32 (15-88)	29 (12-74)	.152
Cooling time (min)	47 (21-120)	45 (18-150)	.218
Aortic valve surgery	12 (23%)	9 (24%)	.946
David operation	2 (4%)	0	.226
Complete arch	1 (2%)	3 (8%)	.168
Composite graft	10 (19%)	3 (8%)	.140
"Elephant trunk"	0	0	
Stent graft	7 (13%)	2 (5%)	.211
Mitral valve surgery	1 (2%)	0	.395
CABG	2 (4%)	4 (11%)	.201
Reoperation	12 (23%)	9 (24%)	.986
30-d Mortality	10 (19%)	2 (5%)	.059
Ventilation time (d)	3 (1-45)	1 (1-14)	.308
ICU stay (h)	5 (1-62)	4 (1-55)	.308
Hospital stay (d)	16 (3-83)	21 (7-88)	.346
Transitory psychotic syndrome	6 (11%)	0	.027
PND	7 (14%)	4 (11%)	.699
TIA	1 (2%)	1 (3%)	.855
Renal failure (requiring dialysis)	5 (9%)	12 (32%)	.013
Multiorgan failure	1 (2%)	0	.376
Reintubation	1 (2%)	1 (3%)	.361
Sepsis	1 (2%)	3 (8%)	.196

Data presented as number (%) or median (range). *ACP,* Antegrade cerebral perfusion; *uACP,* unilateral ACP; *bACP,* bilateral ACP; *CPB,* cardiopulmonary bypass; *CABG,* coronary artery bypass grafting; *ICU,* intensive care unit; *PND,* permanent neurologic deficit; *TIA,* transient ischemic attack.



Survival rates:

	1 year	3 years	5 years
uACP	79%	77%	77%
bACP	90%	81%	73%

Patients at risk:

	1 year	3 years	5 years
uACP	41	32	22
bACP	32	19	7

FIGURE 4. Kaplan-Meier survival analysis curves for unilateral antegrade cerebral perfusion (*uACP*) versus bilateral ACP (*bACP*) (log rank, $P = .885$; median follow-up, 43 months; range, 1-108).

and this has been associated with several complications such as severe bleeding and an intense requirement for blood products.[5]

Although these surgical treatment modalities have not changed dramatically during the past 35 years, the development of better cerebral protection methods has been an important focus of aortic surgical research. In 1990, Ueda and colleagues[7] reported a series of patients with RCP through the superior vena cava during arch exclusion. Coselli and colleagues[16] reported that the mortality (7.9%) and stroke rate (2.4%) of patients undergoing aortic surgery with RCP were favorable. These favorable results were confirmed by other small clinical trials, and the technique of RCP became widely adopted.[17] The technique of ACP had already been described in 1986[6]; however, it only became standard in most centers during the past 5 to 10 years.[6] Although the experience with RCP is now more than 2 decades, controversy still exists about whether RCP has a neuroprotective effect above and beyond that provided by HCA. Some uptake of oxygen during retrograde flow clearly occurs; however, most efforts to document significant improvement in cerebral metabolic function owing to nutritive flow during RCP have failed. Furthermore, experimental studies have shown that significant shunting of blood away from the brain occurs during RCP by way of venovenous anastomoses.[17,18] The only effect that RCP might have is a positive influence on cooling, which helps to protect the brain, especially in patient with insufficient systemic cooling. Although ACP has became the standard approach for an ever-increasing number of centers worldwide,[19] no consensus has been reached among cardiac surgeons concerning the optimal strategy and temperature management for cerebral protection during acute aortic dissection type A surgery. The broad range of preoperative conditions, pathologic anatomic features, complications, and surgical procedures in patients with acute aortic dissection type A and the diversity of CPB strategies has hampered comparisons of postoperative outcomes and the available data.[8] Most publications on this topic have contained data from registries, which have the advantage of including a large number of patients. However, the disadvantage of such registries is that they include data from various centers with several different strategies in operative and anaesthesiologic management.

TABLE 5. Survivors vs nonsurvivors at 30 days

Variable	30-d Survivors	30-d Nonsurvivors	*P* value
Patients (n)	267	62	
Age at surgery (y)	59 (16-87)	65 (32-84)	.023
Male gender	181 (68%)	39 (63%)	.461
Preoperative PRIND	2 (1%)	0	.494
Preoperative TIA	10 (4%)	1 (2%)	.405
Preoperative stroke	7 (3%)	0	.198
Hemodynamic instability	33 (12%)	27 (44%)	<.001
Rupture	111 (42%)	36 (58%)	.019
CPR	2 (1%)	10 (16%)	<.001
Intubated	53 (20%)	17 (27%)	.172
Myocardial infarction	16 (6%)	2 (3%)	.398
Coronary artery disease	37 (14%)	12 (20%)	.173
Arterial hypertension	226 (85%)	53 (87%)	.658
Renal failure	19 (7%)	4 (7%)	.872
Previous cardiac surgery	12 (5%)	7 (11%)	.051
CPB time (min)	179 (101-316)	198 (103-404)	.001
Aortic crossclamp time (min)	108 (61-230)	118 (67-199)	.021
Circulatory arrest time (min)	29 (15-92)	34 (14-88)	.037
Cooling time (min)	55 (18-162)	57 (28-132)	.341
Aortic valve surgery	76 (29%)	22 (36%)	.284
David operation	6 (2%)	0	.234
Complete arch	5 (2%)	2 (3%)	.506
Composite graft	40 (15%)	17 (27%)	.020
"Elephant trunk"	2 (1%)	0	.648
Stent graft	20 (8%)	2 (3%)	.226
CABG	18 (7%)	9 (15%)	.045
Reoperation	73 (28%)	20 (32%)	.130
HCA only	86 (32%)	30 (48%)	.016
RCP	102 (38%)	20 (32%)	.383
ACP	79 (30%)	12 (19%)	.069

Data presented as median (range) or number (%). *PRIND,* Prolonged reversible ischemic neurologic deficit; *TIA,* transient ischemic attack; *CPR,* cardiopulmonary resuscitation; *CPB,* cardiopulmonary bypass; *CABG,* coronary artery bypass grafting; *HCA,* hypothermic circulatory arrest; *RCP,* retrograde cerebral perfusion; *ACP,* antegrade cerebral perfusion.

In the present study, the overall 30-day mortality rate was 19%, similar to that in recent reported studies.[20,21] In-hospital mortality was greater among patients in whom HCA only was used (26%), followed by the RCP group (16%) and 13% in the ACP group. The same was true for

TABLE 6. Multivariate analysis for 30-day mortality

Variable	Wald	*P* value	OR	Regression coefficient	95% CI
Age	4.828	.028	1.026	0.026	1.003-1.051
HCA only	1.321	.250	1.539	0.431	0.738-3.213
ACP	0.321	.571	1.354	0.303	0.475-3.862
Hemodynamic instability	8.970	.003	3.073	1.123	1.474-6.407
CPR	8.732	.003	12.838	2.552	2.362-69.778
Operative year	3.917	.048	0.929	–0.074	0.863-0.999

OR, Odds ratio; *CI,* confidence interval; *HCA,* hypothermic circulatory arrest; *ACP,* antegrade cerebral perfusion; *CPR,* cardiopulmonary resuscitation.

TABLE 7. Permanent neurologic deficit vs none

Variable	PND Yes	PND No	*P* value
Patients (n)	53 (16%)	276 (84%)	
Age at surgery (y)	64 (31-87)	59 (16-85)	.178
Male gender	37 (70%)	183 (66%)	.372
Preoperative PRIND	0	2 (1%)	.710
Preoperative TIA	2 (4%)	9 (3%)	.535
Preoperative stroke	2 (4%)	5 (2%)	.304
Hemodynamic instability	14 (26%)	46 (16%)	.156
Rupture	29 (55%)	118 (43%)	.073
CPR	4 (8%)	8 (3%)	.1
Intubated	15 (28%)	55 (20%)	.125
Myocardial infarction	4 (8%)	14 (5%)	.316
Coronary artery disease	11 (21%)	38 (14%)	.142
Arterial hypertension	47 (89%)	232 (84%)	.283
Renal failure	1 (2%)	22 (8%)	.091
Previous cardiac surgery	2 (4%)	17 (6%)	.378
CPB time (min)	179 (101-304)	180 (101-404)	.704
Aortic crossclamp time (min)	107 (62-205)	110 (61-230)	.455
Circulatory arrest time (min)	31 (14-72)	30 (12-92)	.517
Cooling time (min)	55 (28-143)	56 (18-162)	.572
Aortic valve surgery	12 (23%)	86 (31%)	.136
David operation	0	6 (2%)	.345
Complete arch	3 (6%)	4 (1%)	.086
Composite graft	9 (17%)	48 (17%)	.562
"Elephant trunk"	2 (4%)	0	.026
Stent graft	2 (4%)	20 (7%)	.279
Mitral valve surgery	0	3 (1%)	.589
CABG	6 (11%)	21 (8%)	.255
Reoperation	24 (45%)	70 (25%)	.006
HCA only	27 (51%)	89 (32%)	.008
RCP	15 (28%)	107 (39%)	.097
ACP	11 (21%)	80 (29%)	.144
uACP	7 (13%)	45 (16%)	.468
bACP	4 (8%)	34 (12%)	.468
Liver failure	4 (8%)	4 (1%)	.026
Pulmonary failure	10 (19%)	19 (7%)	.010
Renal failure (requiring dialysis)	16 (30%)	37 (13%)	.06
Multiorgan failure	5 (9%)	20 (7%)	.409
Sepsis	15 (28%)	24 (9%)	<.001

Data presented as median (range) or number (%). *PND,* Permanent neurologic deficit; *PRIND,* prolonged reversible ischemic neurologic deficit; *TIA,* transient ischemic attack; *CPR,* cardiopulmonary resuscitation; *CPB,* cardiopulmonary bypass; *CABG,* coronary artery bypass grafting; *HCA,* hypothermic circulatory arrest; *RCP,* retrograde cerebral perfusion; *ACP,* antegrade cerebral perfusion; *uACP,* unilateral ACP; *bACP,* bilateral ACP.

long-term survival. RCP showed major improvement in reducing mortality and PND but failed to show benefit in avoiding temporary neurologic dysfunction. In contrast, ACP, not only was associated with the lowest hospital mortality and PND, but also showed a benefit in reducing the occurrence of transient postoperative neurologic deficits. Similar results were found by Okita and colleagues[22] from Japan.

The significantly lower hospital mortality rate and PND using ACP compared with RCP or HCA alone in the present

TABLE 8. Multivariate analysis for permanent neurologic deficit

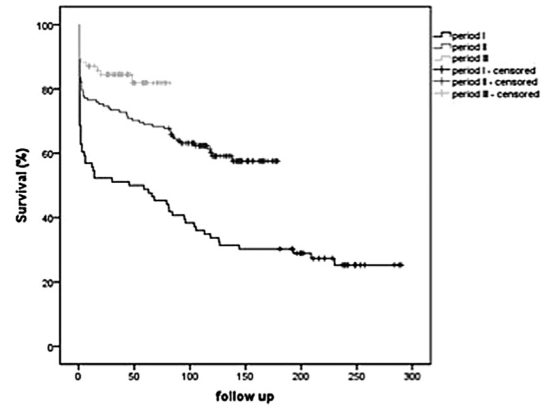
Variable	Wald	*P* value	Regression coefficient	OR	95% CI
Age	2.703	.100	0.019	1.019	0.996-1.042
HCA only	2.143	.143	0.519	1.681	0.839-3.370
Previous cardiac surgery	0.897	.343	–0.745	0.475	0.102-2.217
Operative year	3.536	.060	–0.058	0.944	0.888-1.002

OR, Odds ratio; *CI,* confidence interval; *HCA,* hypothermic circulatory arrest.

study has shown the superior cerebral protection provided by ACP when prolonged and acute operations on the thoracic aorta are undertaken.

In our study, we not only compared the 3 basic methods of cerebral protection, but also performed a subgroup analysis of bACP versus uACP. Although, basically the outcomes in these 2 groups were not significantly different, there seemed to be at least a trend toward better 30-day survival in the bACP group. Nevertheless, this result could have been biased because during the introduction period of ACP in our center, we did not use near infrared spectroscopy for continuous neuromonitoring. Therefore, it is possible that a few of the uACP patients showed a decrease in oxygen saturation in the near infrared spectroscopy. In the last years of the study, we have advocated uACP with continuous neuromonitoring, with the possibility of switching to bACP in the case of left hemispheric cerebral malperfusion, as the procedure of choice for cerebral protection in patients undergoing surgery for aortic arch pathologic findings.

Only hemodynamic instability, preoperative cardiopulmonary resuscitation, patient age, and operative year were statistically significant independent risk factors for



Survival rates

	1-years	3-years	5-years	10-years
Period I	56%	51%	49%	34%
Period II	77%	73%	70%	59%
Period III	87%	85%	8%	n.a.

Patients at risk

	1-years	3-years	5-years	10-years
Period I	48	44	42	29
Period II	121	116	109	52
Period III	70	46	29	n.a.

FIGURE 5. Survival rates in 3 different eras of aortic surgery (log rank, $P < .001$).

mortality in our patient population. This was not surprising, and results reported by others would lead to the expectation that patients with frank rupture and hemodynamic compromise would have a worse outcome than patients who were stable preoperatively. Also not surprisingly, older patients with such aortic pathologic findings had worse outcomes than younger patients.

That concomitant procedures failed to have any effect on mortality was also reassuring, suggesting that the current approach at our institution, which involves resecting the site of the intimal tear and performing adjunctive procedures when clinically indicated, is a reasonable method to treat acute dissection in a setting in which aneurysm surgery is a routine procedure. The use of the Bentall-de Bono procedure depended on the degree of aortic valve insuffciency and the judgment of the surgeon of whether a competent valve could be achieved by resuspension. However, various approaches to the aortic valve—leaving it untouched, replacing it, or resuspending the valve leaflets—also had no effect on mortality. It is possible, however, that some aspects of these results might not easily be extrapolated to institutions with less experience with dissection and aneurysms. It must be emphasized that the principal object of emergency surgery for acute dissection must be the immediate survival of the patient, and more limited

TABLE 9. Study periods for type A aortic dissection surgery

Variable	Period 1 (1987-1996)	Period 2 (1997-2004)	Period 3 (2005-January 2011)	*P* value
Patients (n)	86	158	85	
Age (y)	57 (16-81)	59 (18-87)	62 (33-85)	.183
Male gender	59 (67%)	97 (61%)	64 (75%)	.083
Preoperative hemodynamic instability	19 (22%)	33 (21%)	8 (9%)	.052
CPR	3 (3%)	7 (4%)	2 (2%)	.712
Rupture	37 (43%)	91 (58%)	19 (22%)	<.001
PND	23 (27%)	21 (13%)	9 (11%)	.007
30-d Mortality	27 (31%)	26 (16%)	9 (11%)	.001
HCA only	64 (74%)	43 (27%)	9 (11%)	<.001
ICU stay	6 (1-86)	6 (1-62)	5 (1-63)	.667
RCP	22 (26%)	89 (56%)	11 (13%)	<.001
ACP	0	26 (16%)	65 (76%)	<.001

Data presented as median (range) or number (%). *CPR,* Cardiopulmonary resuscitation; *PND,* permanent neurologic deficit; *HCA,* hypothermic circulatory arrest; *ICU,* intensive care unit; *RCP,* retrograde cerebral perfusion; *ACP,* antegrade cerebral perfusion.

operations could be more appropriate under particular circumstances.

Study Limitations

The major limitation of the present study was that all data were analyzed retrospectively, a process that mandates caution in the interpretation of the results. Factors such as the ''learning curve'' of each surgeon during the study period and improvement in intra- and postoperative care cannot be considered in a retrospective study. Particularly because of the long observation period, it was very difficult to identify strong independent predictors of mortality or PND. This limitation was strongly supported by the finding that including the operative year in the multivariate analysis removed every other independent predictor for PND, leaving only age, cardiopulmonary resuscitation, and hemodynamic instability as predictors of mortality. During the past decades, not only have the surgical technique and neuroprotective methods improved, but also better anesthesetic management, earlier and better diagnosis of the disease, accelerated transfer to the operating room, and a higher awareness of the transferring physicians of the disease are factors that have led to significant improvements in the outcomes of patients undergoing surgery for type A aortic dissection.

CONCLUSIONS

Patients in the ACP group had the best short- and long-term survival in our series. However, owing to the rather long study period, several improvements in the treatment of patients with type A aortic dissection have been achieved. Therefore, it was difficult to identify ACP as favorable predictor. Patients in the HCA-only group had significantly greater rates of PND. However, on multivariate regression analysis, HCA could not be identified as an independent predictor of PND. Finally, 30-day mortality was mainly influenced by the preoperative hemodynamic status, with hemodynamic instability resulting in greater mortality.

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TABLE E1. Cause of death (30-day mortality)

Cause of death	Patients (n = 62)
Cardiac failure	24
Multiorgan failure	14
Bleeding	9
Neurologic complications	7
Sepsis	5
Pulmonary failure	2
Unknown	1